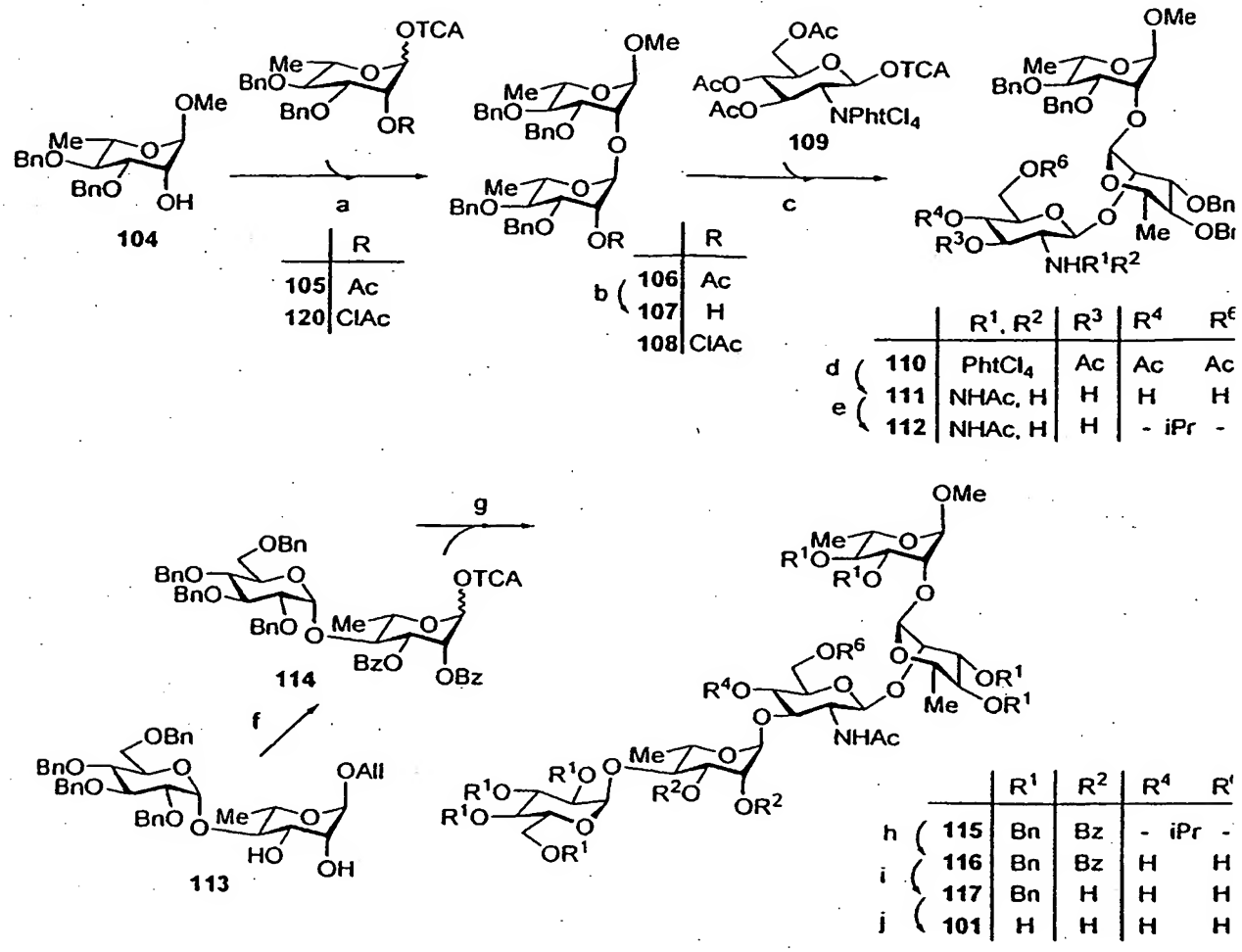


a. TMSOTf, Et_2O, –35°C → rt; *b.* MeONa, MeOH-CH_2Cl_2, rt; *c.* $Sn(OTf)_2$, CH_3CN, rt; *d. i.* $H_2NCH_2CH_2NH_2$, EtOH, 60°C, *ii.* Ac_2O, EtOH; *iii.* MeONa, MeOH-CH_2Cl_2, rt; *e.* $Me_2C(OMe)_2$, PTSA, acetone, rt; *f.* see ref (L. A. Mulard, C. Costachel, P. J. Sansonetti, *J. Carbohydr. Chem.* **2000**, *19*, 849-877); *g.* 4Å-MS, TfOH, CH_2Cl_2, –15°C → rt; *h.* 90% aq TFA, 0°C; *i.* MeONa, MeOH-CH_2Cl_2, rt ; *j.* H_2, 10% Pd/C, EtOH-AcOH, rt.

FIGURE 1

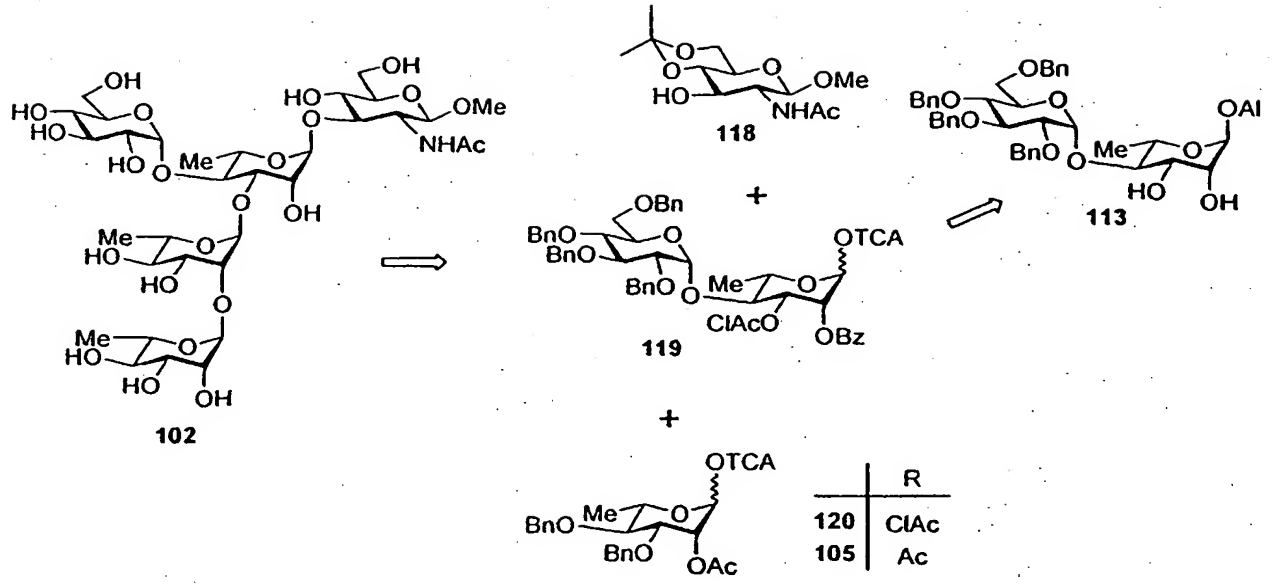
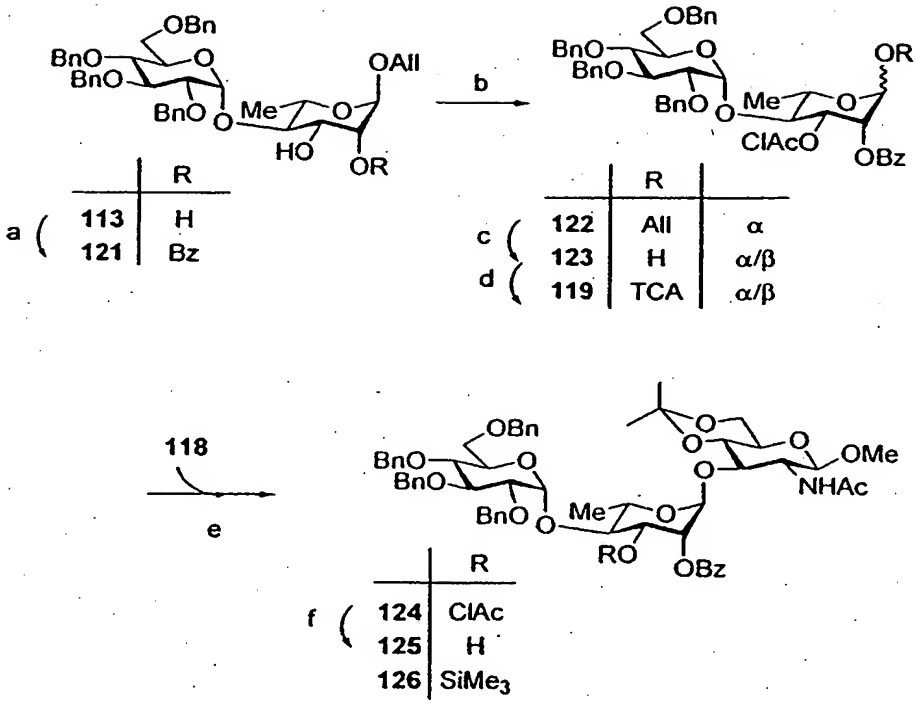
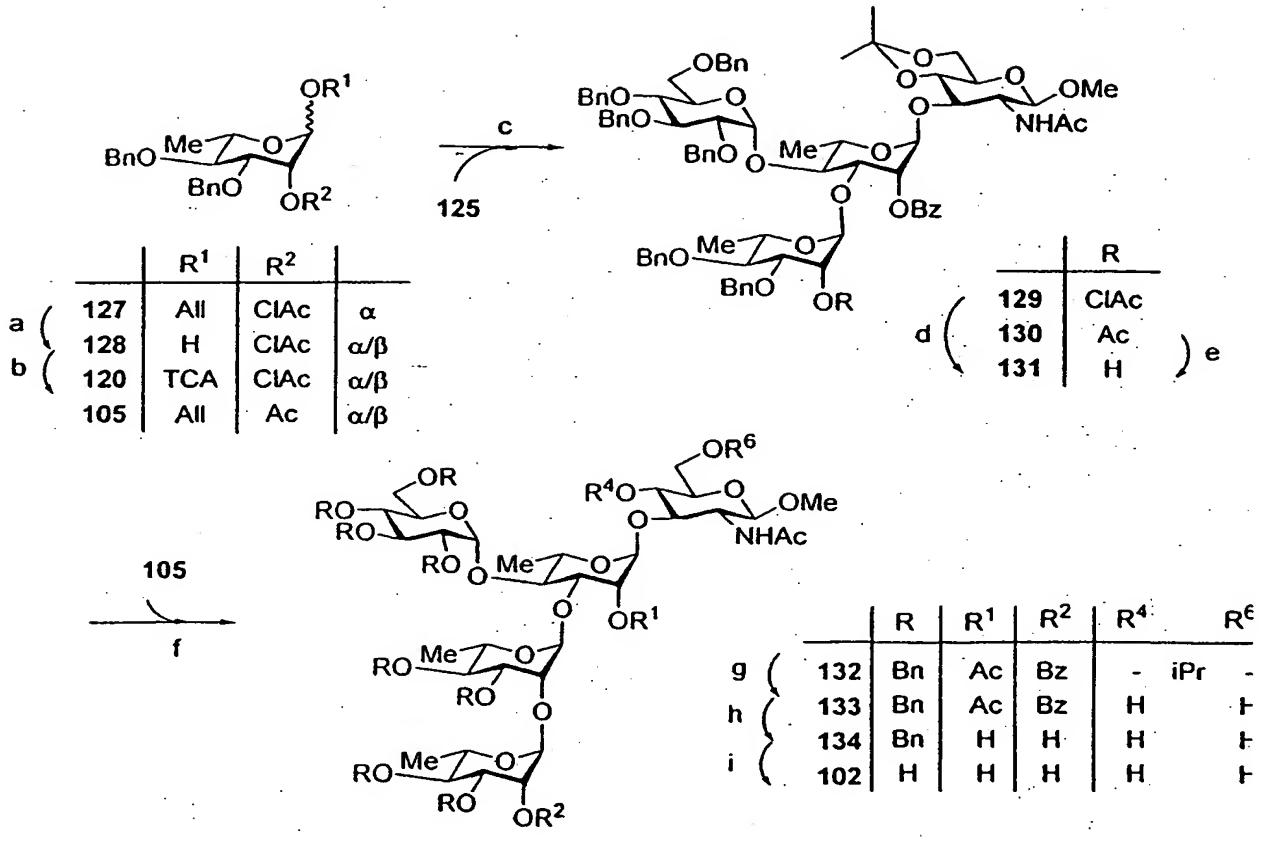


FIGURE 2



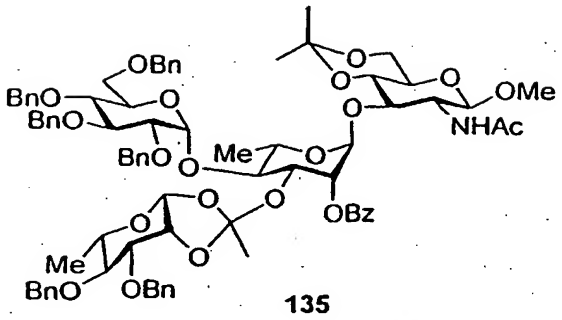
a. see ref. (F. Segat, L. A. Mulard, *Tetrahedron: Asymmetry* **2002**, *13*, 2211-2222); *b.* $(ClAc)_2O$, Pyridine-CH_2Cl_2, 0°C; *c. i.* $(COD)Ir^+(P(MePh_2)_2)PF_6^-$, THF, *ii.* I_2, THF, rt; *d.* CCl_3CN, DBU, CH_2Cl_2, 0°C; *e.* 4Å-MS, TMSOTf, CH_2Cl_2, –60°C → rt; *f.* thiourea, MeOH-pyridine, 65°C.

FIGURE 3



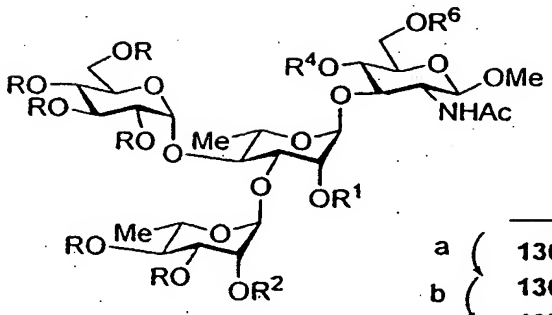
a. i. $(COD)Ir^{+}(P(MePh_2)_2)PF_6^{-}$, THF, ii. I_2, THF, rt; *b.* CCl_3CN, K_2CO_3, CH_2Cl_2, 0°C; *c.* TMSOTf, Et_2O, –60°C → 0°C; *d.* thiourea, MeOH-pyridine, 65°C; *e.* guanidine, EtOH-CH_2Cl_2, rt; *f.* 4Å-MS, TMSOTf, Et_2O, –60°C → rt; *g.* 50% aq TFA, CH_2Cl_2, 0°C; *h.* 0.5M MeONa, MeOH, 55°C; *i.* 10% Pd/C, EtOH-EtOAc, 1M aq HCl, rt.

FIGURE 4



135

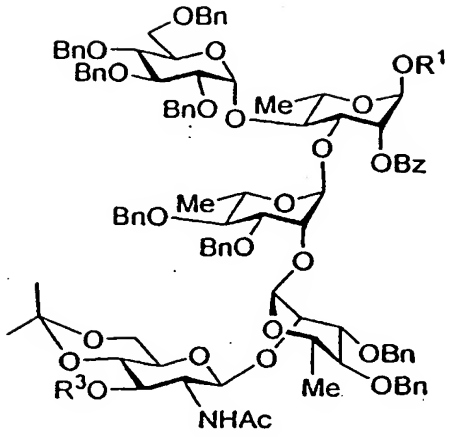
FIGURE 5



		R	R^1	R^2	R^4	R^6
a	130	Bn	Ac	Bz	- iPr	-
b	136	Bn	Ac	Bz	H	H
	137	Bn	H	H	H	H
c	103	H	H	H	H	H

a. 50% aq TFA, CH_2Cl_2, 0°C; *b.* MeONa, MeOH, 55°C; *c.* 10% Pd/C, EtOH-EtOAc, 1M aq HCl, rt.

FIGURE 6



	R^1	R^3
201	All	All
202	All	H
203	TCA	Ac

FIGURE 7

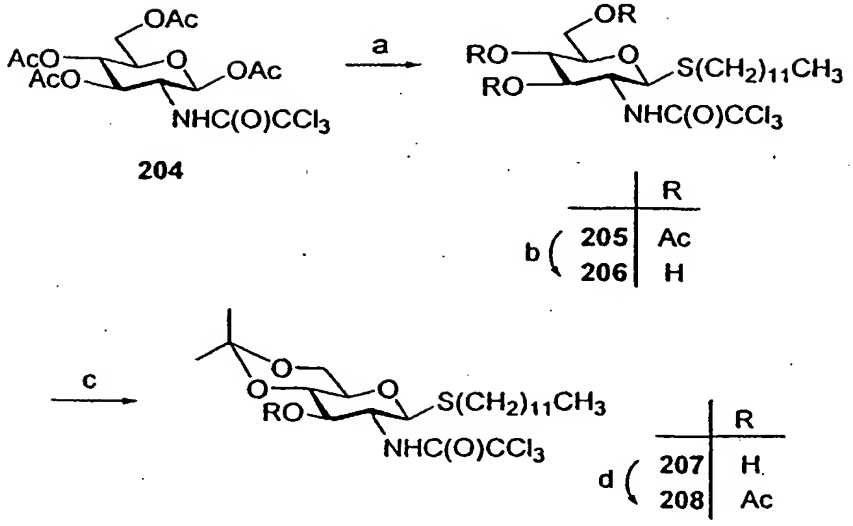
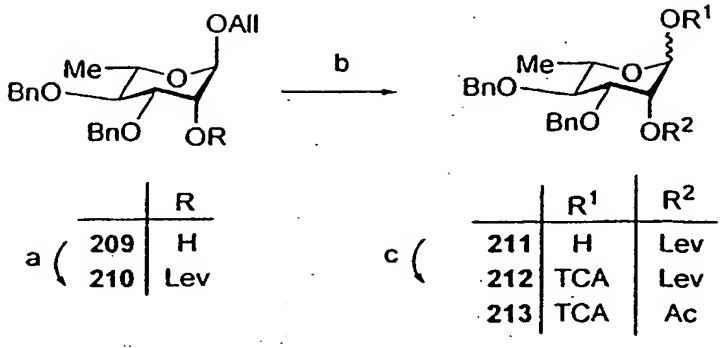


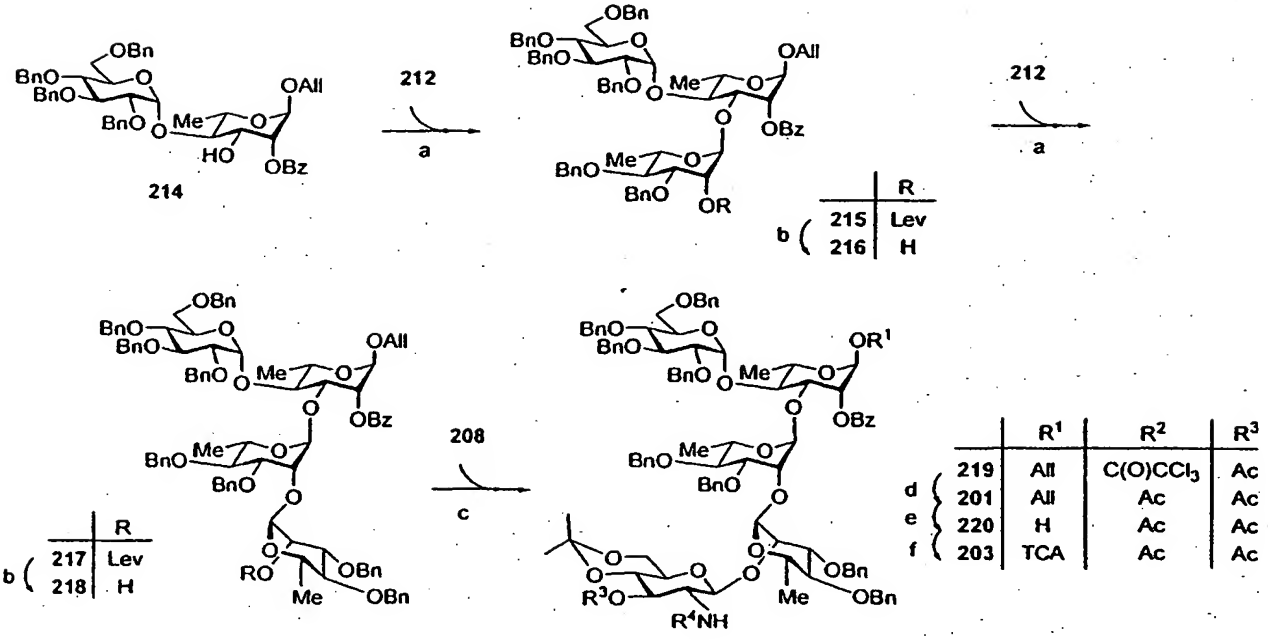
FIGURE 8



		R
a	209	H
	210	Lev

		R1	R2
c	211	H	Lev
	212	TCA	Lev
	213	TCA	Ac

FIGURE 9



		R
b	215	Lev
	216	H

		R
b	217	Lev
	218	H

		R1	R2	R3
d	219	All	$C(O)CCl_3$	Ac
	201	All	Ac	Ac
e	220	H	Ac	Ac
f	203	TCA	Ac	Ac

FIGURE 10

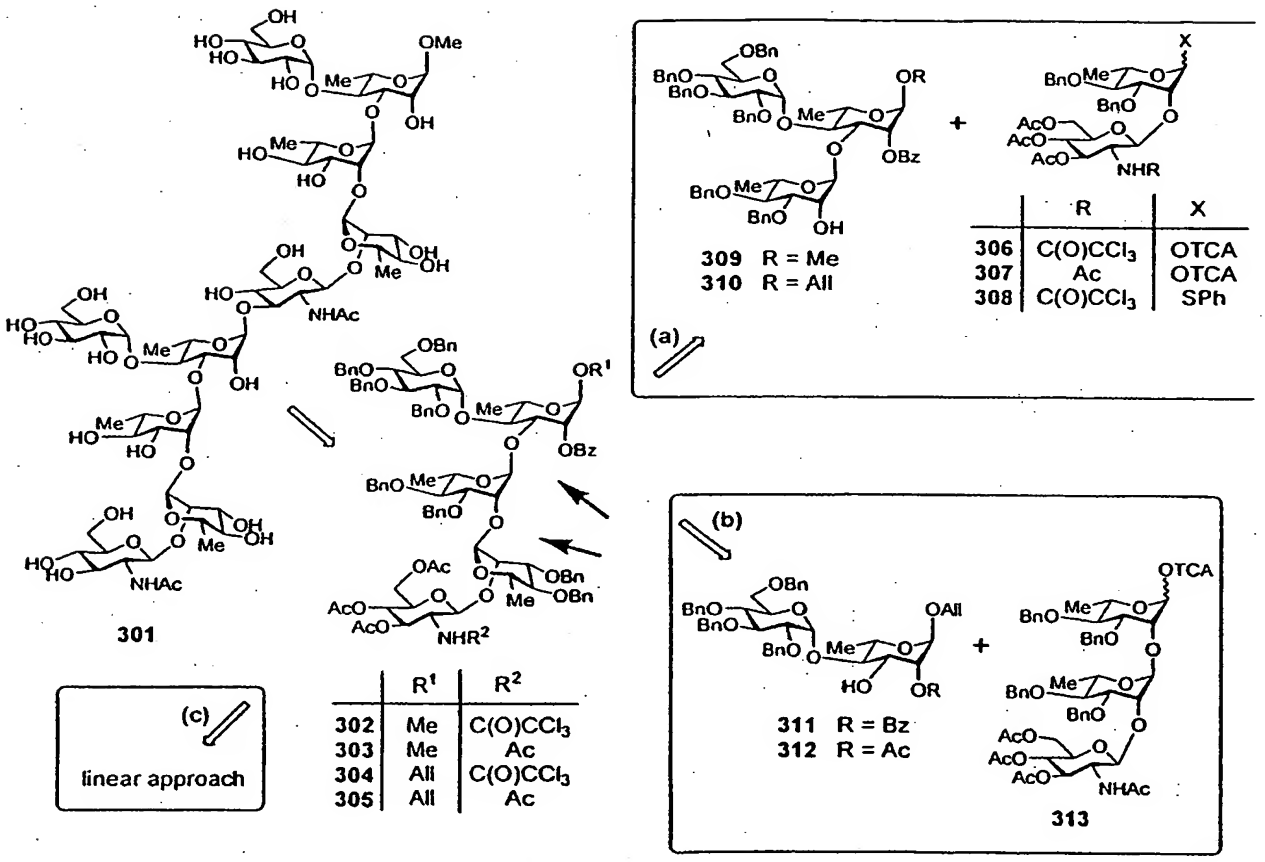
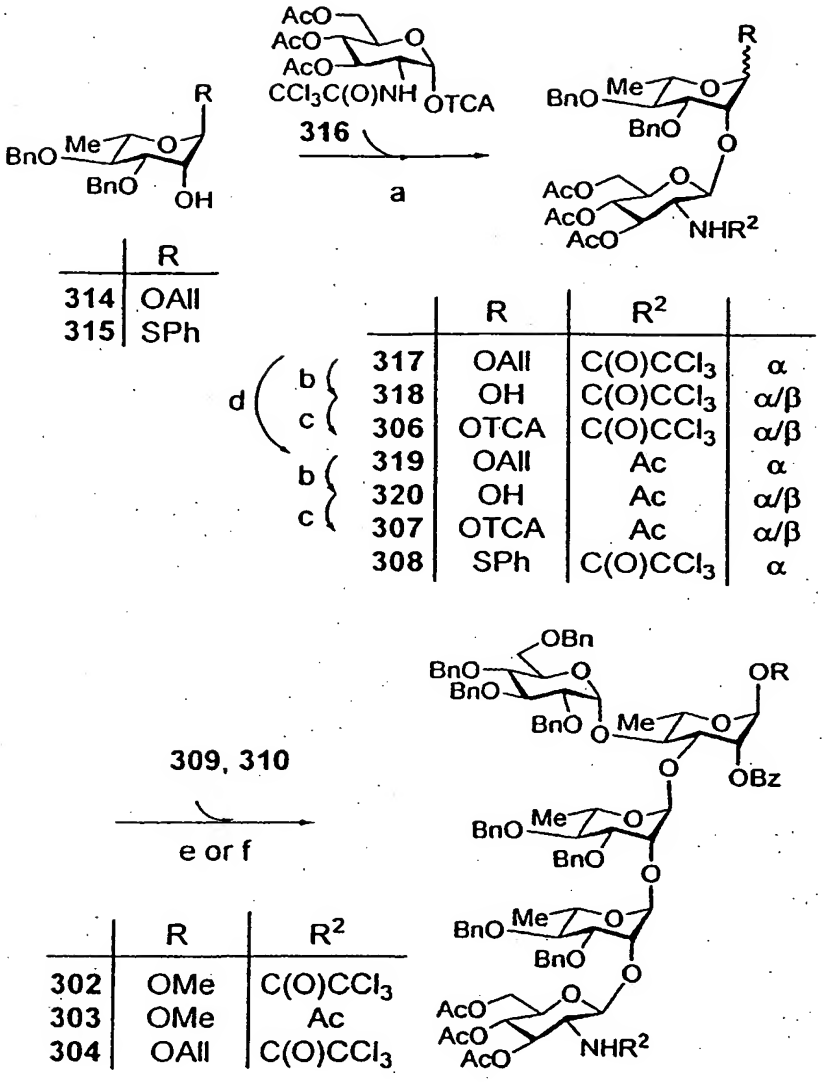

301
(a)
309 R = Me
310 R = All
R X
306 C(O)CCl3 OTCA
307 Ac OTCA
308 C(O)CCl3 SPh
(b)
311 R = Bz
312 R = Ac
313
(c)
linear approach
R1 R2
302 Me C(O)CCl3
303 Me Ac
304 All C(O)CCl3
305 All Ac

FIGURE 11



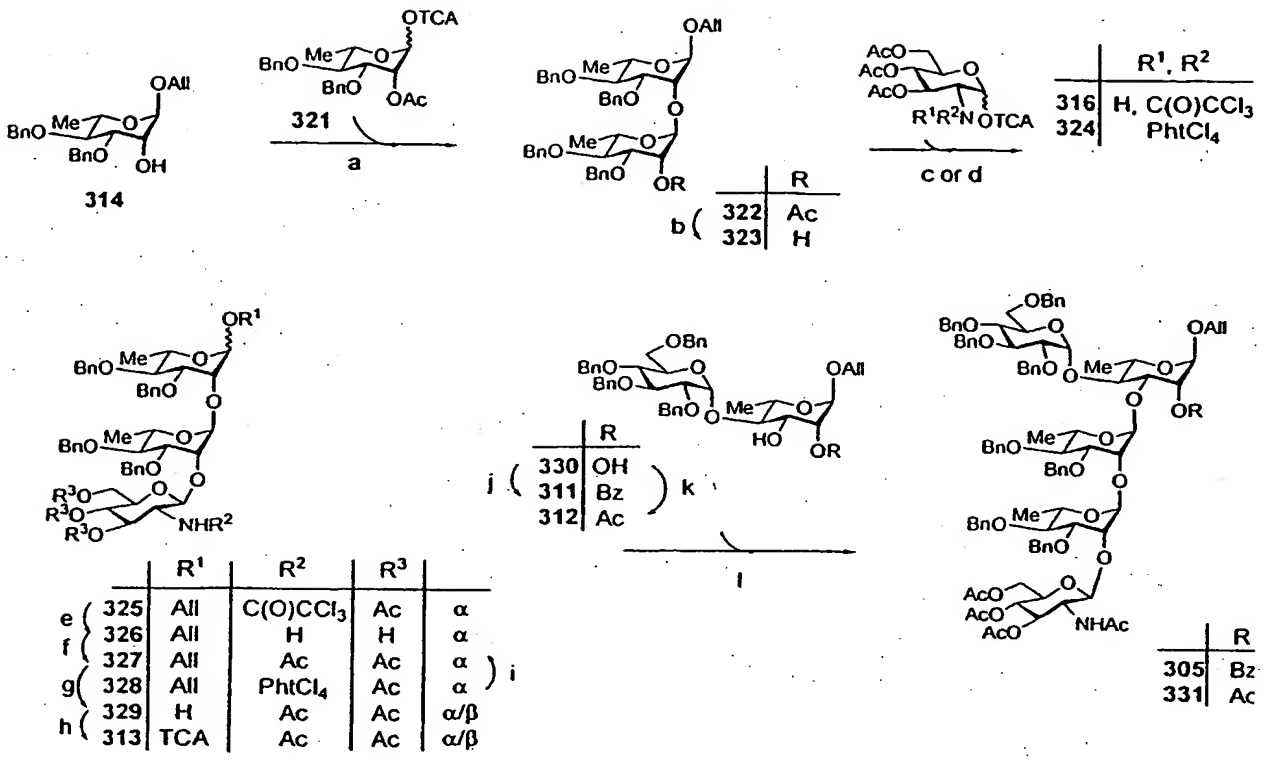
	R
314	OAll
315	SPh

	R	R^2	
317	OAll	$C(O)CCl_3$	α
318	OH	$C(O)CCl_3$	α/β
306	OTCA	$C(O)CCl_3$	α/β
319	OAll	Ac	α
320	OH	Ac	α/β
307	OTCA	Ac	α/β
308	SPh	$C(O)CCl_3$	α

	R	R^2
302	OMe	$C(O)CCl_3$
303	OMe	Ac
304	OAll	$C(O)CCl_3$

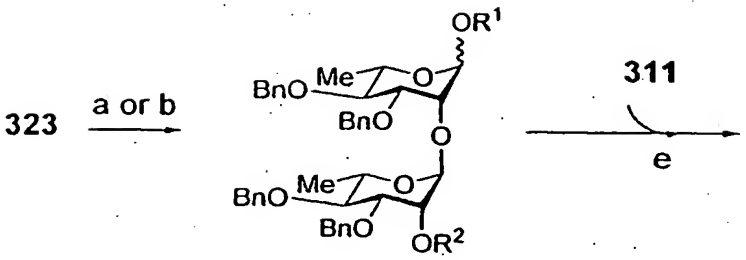
(a) cat. TMSOTf, anhydrous DCM, 0.5 h, 0°C, 97% (**308**), 99% (**317**); (b) i. cat. $[Ir(COD)\{PCH_3(C_6H_5)_2\}_2]^+PF_6^-$, THF, rt, 20 h, ii. HgO, $HgCl_2$, acetone/water, rt, 2 h, 81% (**318**), 69% (**320**); (c) CCl_3CN, DBU, DCM, 0°C, 1 h, 78% (**306**), 86% (**7**); (d) i. NH_3, MeOH, 20h, 0°C, ii. Ac_2O, MeOH, iii. Ac_2O, Py, 90%; (e) cat. TMSOTf, CH_3CN, 0°C, 41% (**2**); (f) cat. TfOH, NIS, Et_2O, DCE, 0°C, 10% (**304**).

FIGURE 12

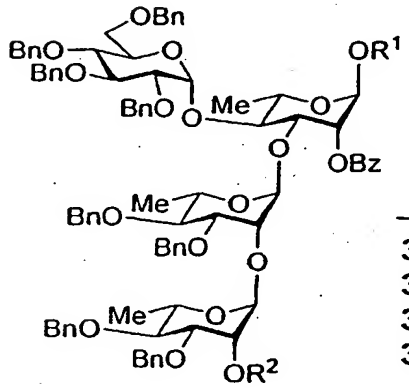


(a) cat. TMSOTf, anhydrous Et_2O, 3 h, –55 → –20°C, 92%; (b) MeONa, MeOH, 3 h, rt, 93%; (c) cat. TMSOTf, 4Å molecular sieves, DCE, 3 h, –20 → 0°C, 96%; (d) cat. TMSOTf, anhydrous Et_2O, 4 h, 0°C → rt, 65%; (e) i. MeONa, MeOH, Et_3N, rt, 18 h, rt, ii. Ac_2O, 0.5 h, 0°C → rt, 45%; (f) Py, Ac_2O, 18 h, 0°C → rt, 94%; (g) i. cat. $[Ir(COD)\{PCH_3(C_6H_5)_2\}_2]^+PF_6^-$, THF, rt, 20 h, ii. HgO, $HgCl_2$, acetone/water, rt, 2 h, 83%; (h) CCl_3CN, DBU, DCM, 0°C, 40 min, 94%; (i) i. ethylenediamine, THF, EtOH, 55°C, 4 h, ii. Ac_2O, rt, 1.5 h, iii. Py, Ac_2O, 0°C, overnight, 68%; (j) i. $PhC(OMe)_3$, CSA, DCM, ii. 50% aq. TFA, DCM, 87%; (k) i. $MeC(OMe)_3$, CSA, DCM, ii. 50% aq. TFA, DCM, 90%; (l) $BF_3.Et_2O$, anhydrous Et_2O, 4Å molecular sieves, 0°C → rt, 18 h, 44%.

FIGURE 13



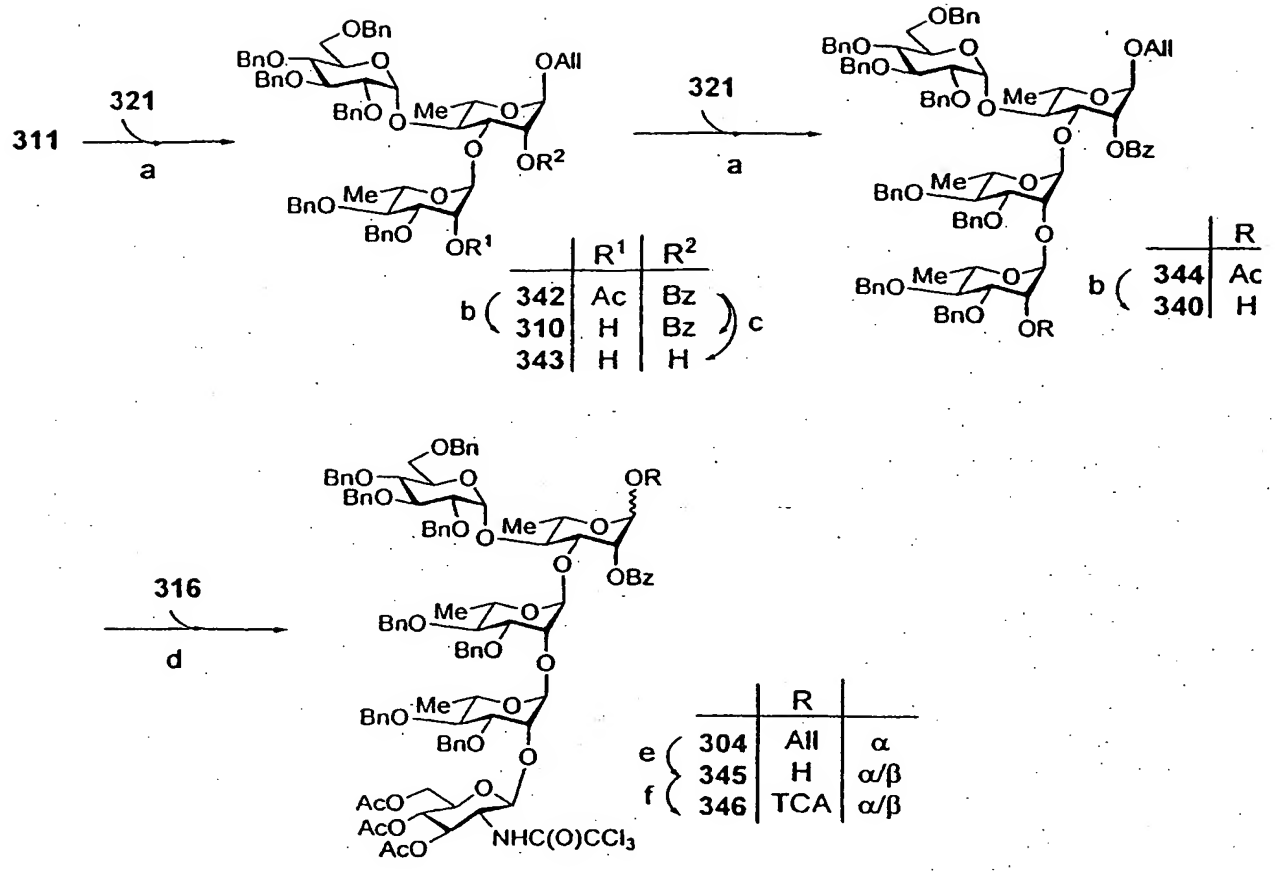
		R^1	R^2	
c	332	All	ClAc	α
d	333	H	ClAc	α/β
	334	TCA	ClAc	α/β
c	335	All	*p*MeOBn	α
d	336	H	*p*MeOBn	α/β
	337	TCA	*p*MeOBn	α/β



	R^1	R^2
338	All	ClAc
339	All	*p*MeOBn
340	All	H
341	Me	Ac

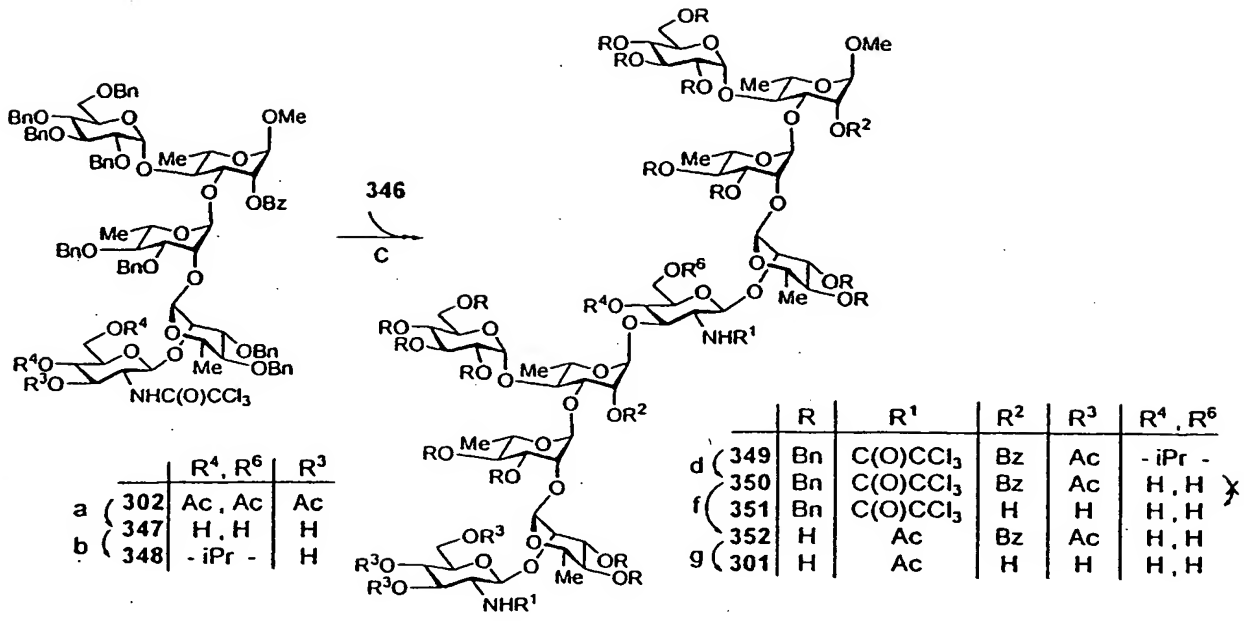
(a) $ClAc_2O$, Py, 0°C → rt, overnight, 57%; (b) *p*MeOBnCl, NaH, DMF, rt, overnight, 97%; (c) i. cat. $[Ir(COD)\{PCH_3(C_6H_5)_2\}_2]^+PF_6^-$, THF, rt, 20 h, ii. HgO, $HgCl_2$, acetone/water, rt, 2 h, 84% (333), 73% (336); (d) CCl_3CN, DBU, DCM, 0°C, 1 h, 83% (334), 82% (337); (e) cat. TMSOTf, anhydrous Et_2O, –60°C → rt, overnight, 22% (338), 44% (339).

FIGURE 14



(a) cat. TMSOTf, anhydrous Et_2O, –50°C → rt, overnight, 84% (**342**), 90% (**344**); (b) HBF_4/Et_2O, MeOH, rt, 4 days, 84% (**310**), 84% (**340**); (c) Guanidine, DCM, rt; (d) cat. TMSOTf, anhydrous DCM, 4Å molecular sieves, 0°C → rt, 3 h, 98%; (e) i. cat. $[Ir(COD)\{PCH_3(C_6H_5)_2\}_2]^+PF_6^-$, THF, rt, 20 h, ii. HgO, $HgCl_2$, acetone/water, rt, 2 h; (f) CCl_3CN, DBU, DCM, 0°C, 1 h, 66% (2 steps).

FIGURE 15



		R^4, R^6	R^3
a	302	Ac, Ac	Ac
b	347	H, H	H
	348	- iPr -	H

		R	R^1	R^2	R^3	R^4, R^6
d	349	Bn	$C(O)CCl_3$	Bz	Ac	- iPr -
	350	Bn	$C(O)CCl_3$	Bz	Ac	H, H
f	351	Bn	$C(O)CCl_3$	H	H	H, H
	352	H	Ac	Bz	Ac	H, H
g	301	H	Ac	H	H	H, H

(a) MeONa, MeOH, rt, 0.5 h; (b) 2-methoxypropene, CSA, DMF, 72% (2 steps); (c) cat. TfOH, anhydrous DCE, 4Å molecular sieves, –35°C → –10°C, 2.5 h; (d) TFA, water/DCM, 0°C, 3 h, 72% (2 steps); (e) MeONa, MeOH, DCM, 55°C; (f) i. H_2, Pd/C, EtOH, EtOAc, 1M HCl, rt, 72 h, ii. H_2, Pd/C, MeOH, Et_3N, rt, 24 h. (g) MeONa, MeOH, DCM, 55°C, overnight, 37% (3 steps).

FIGURE 16

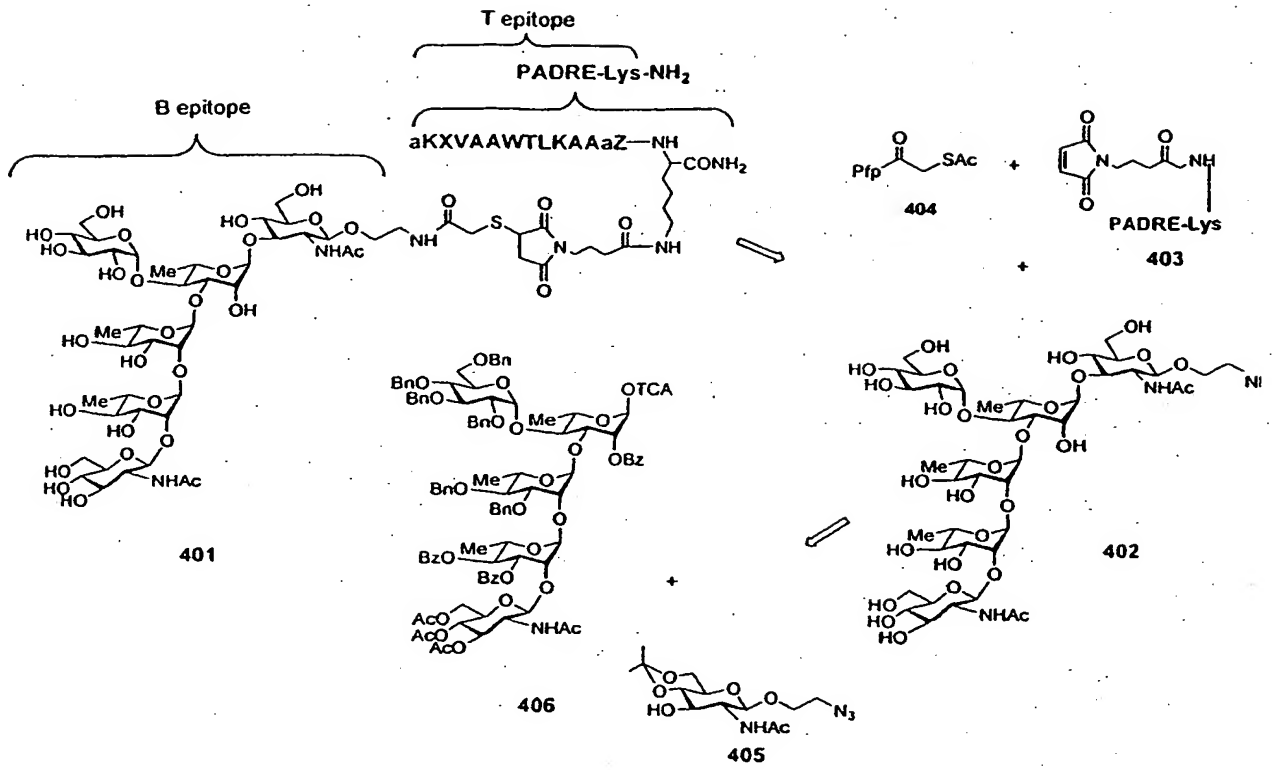
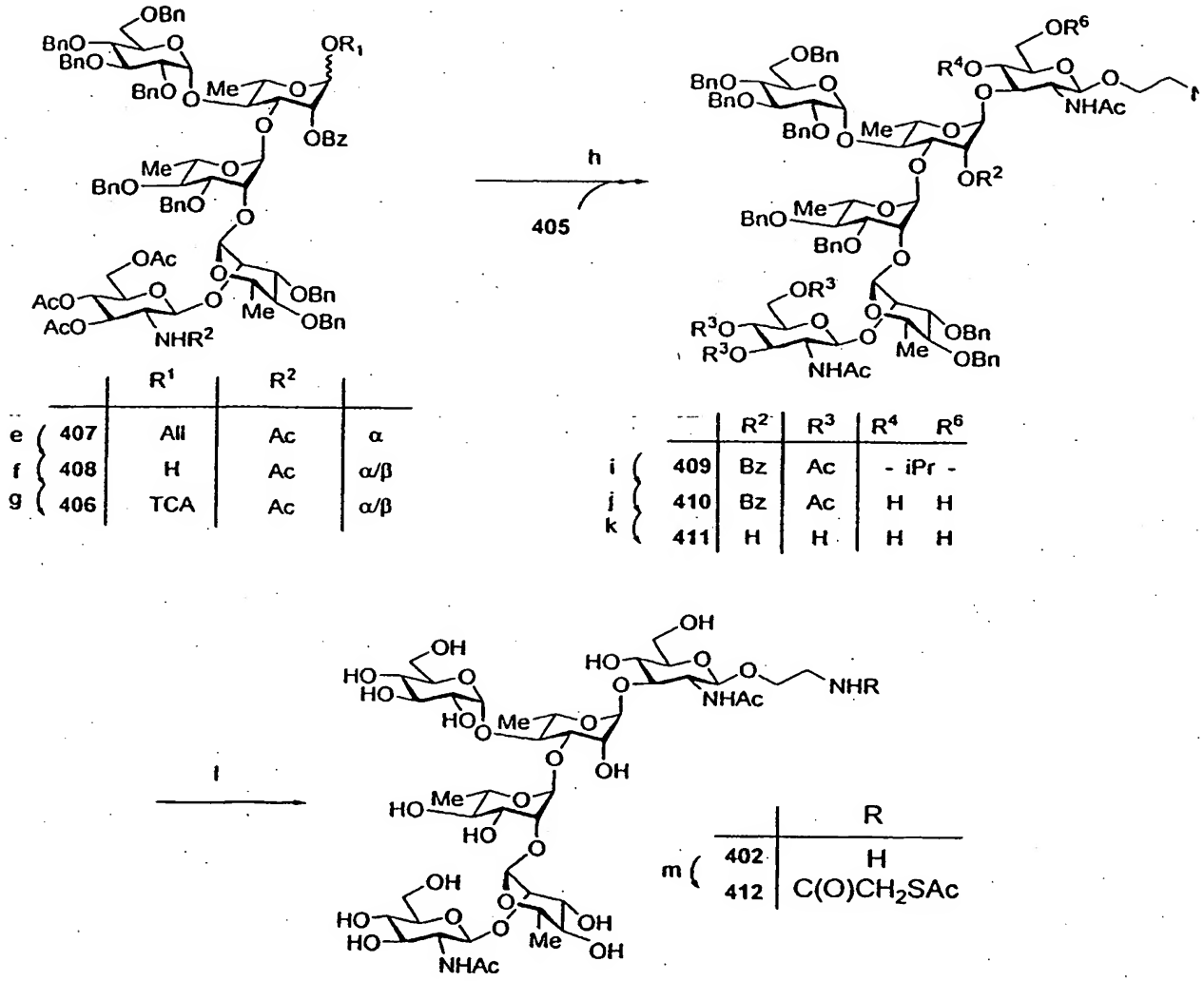

T epitope
PADRE-Lys-NH2
B epitope
aKXVAAWTLKAAaZ—NH
CONH2
Pfp
SAc
404
PADRE-Lys
403
401
406
405
402

FIGURE 17



		R^1	R^2	
e	407	All	Ac	α
f	408	H	Ac	α/β
g	406	TCA	Ac	α/β

		R^2	R^3	R^4	R^6
i	409	Bz	Ac	- iPr	-
j	410	Bz	Ac	H	H
k	411	H	H	H	H

		R
m	402	H
	412	$C(O)CH_2SAc$

FIGURE 18

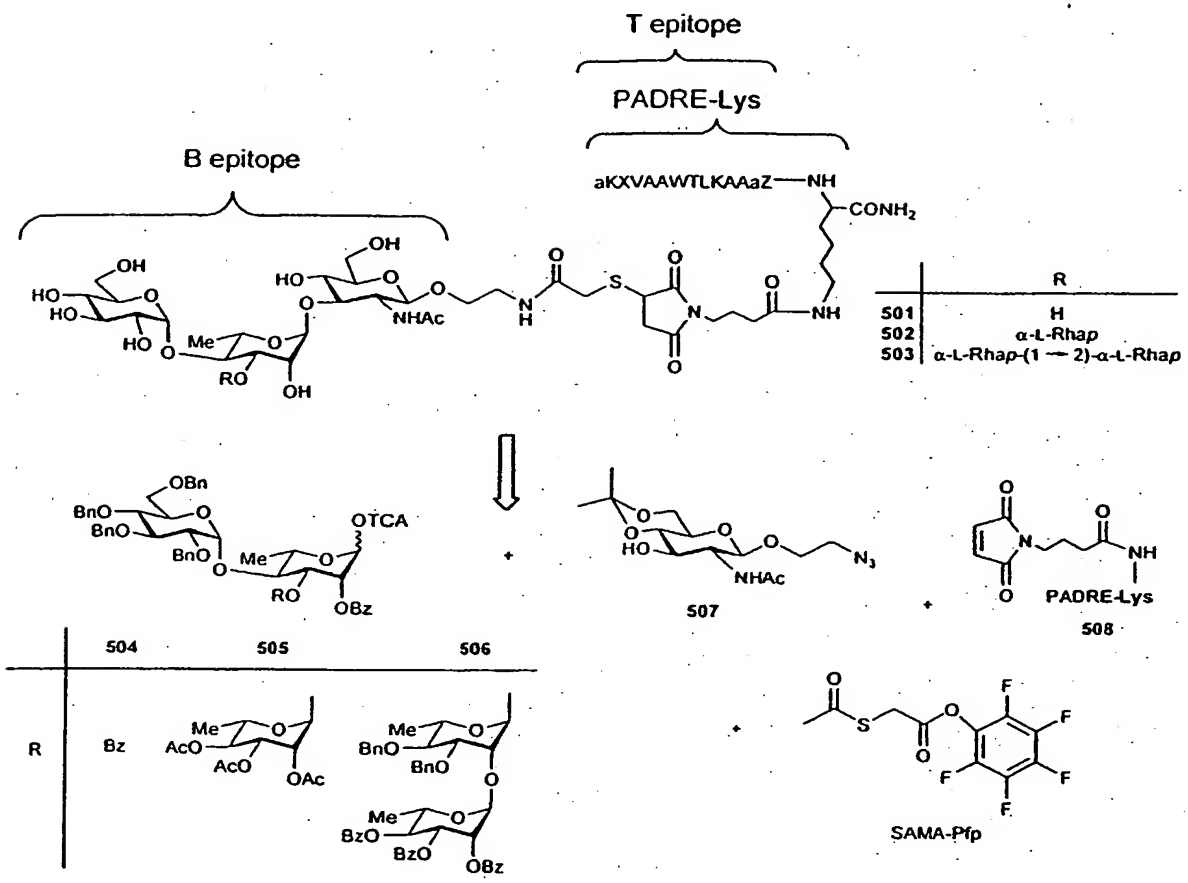

T epitope
PADRE-Lys
B epitope
aKXVAAWTLKAAaZ—NH
CONH2
R
501 H
502 α-L-Rhap
503 α-L-Rhap-(1 → 2)-α-L-Rhap
504 505 506
R
Bz
507
508
PADRE-Lys
SAMA-Pfp

FIGURE 19

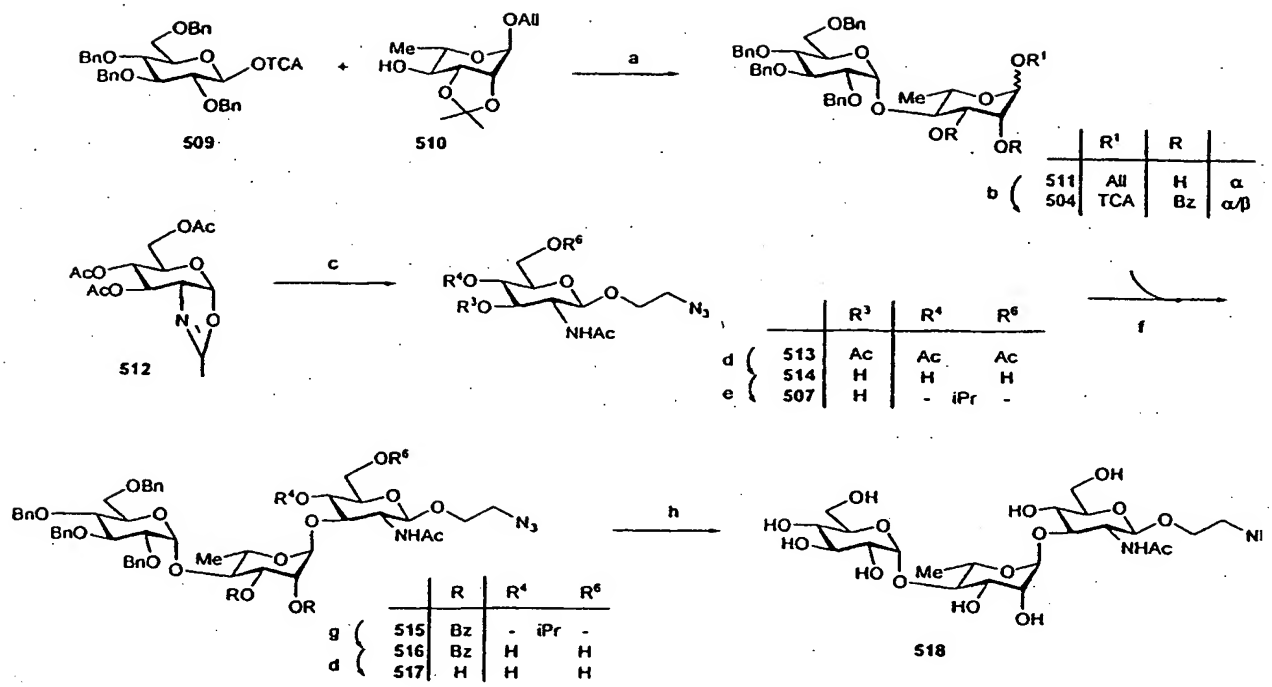

509
510
a
511 All H α
504 TCA Bz α/β
b
512
c
513 Ac Ac Ac
514 H H H
507 H - iPr -
d
e
f
515 Bz - iPr -
516 Bz H H
517 H H H
g
d
h
518

FIGURE 20

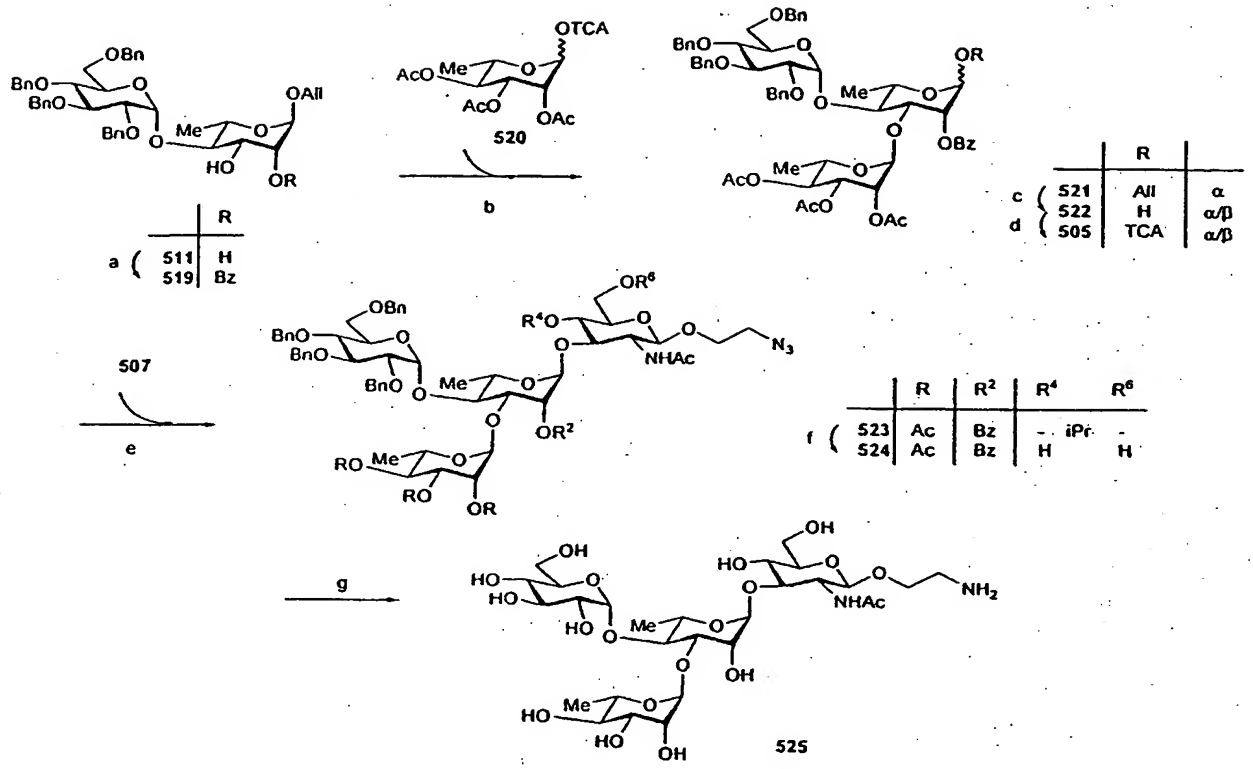

OBn
BnO
BnO
BnO
Me
HO
OAll
OR
R
a
511 H
519 Bz
OTCA
AcO
Me
AcO
OAc
520
b
OBn
BnO
BnO
BnO
Me
OR
OBz
AcO
Me
AcO
OAc
c
d
R
521 All α
522 H α/β
505 TCA α/β
507
e
OR6
R4O
NHAc
N3
OR2
RO
Me
RO
OR
f
R R2 R4 R6
523 Ac Bz iPr -
524 Ac Bz H H
g
OH
HO
HO
HO
Me
NHAc
NH2
OH
HO
Me
HO
OH
525

FIGURE 21

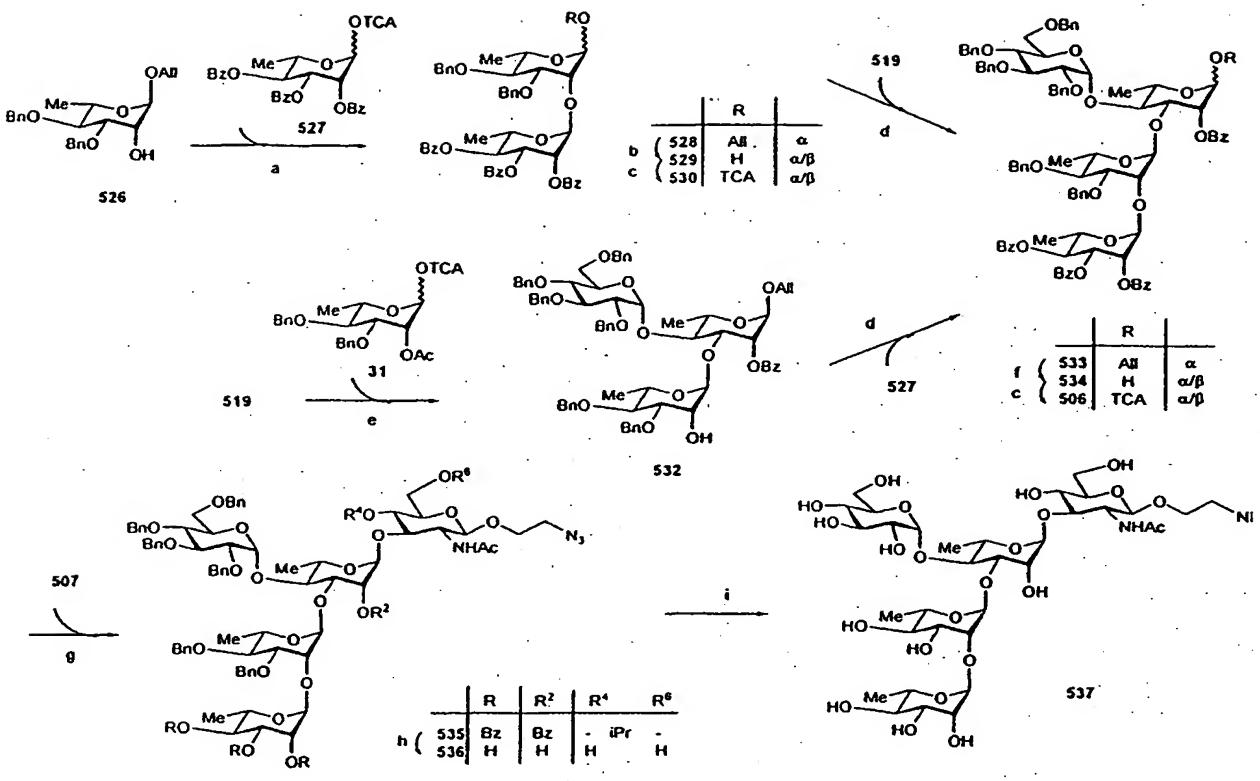

526
527
a
528 All α
529 H α/β
530 TCA α/β
519
d
533 All α
534 H α/β
506 TCA α/β
31
519
e
532
527
507
g
535 Bz Bz - iPr -
536 H H H H
h
i
537

FIGURE 22

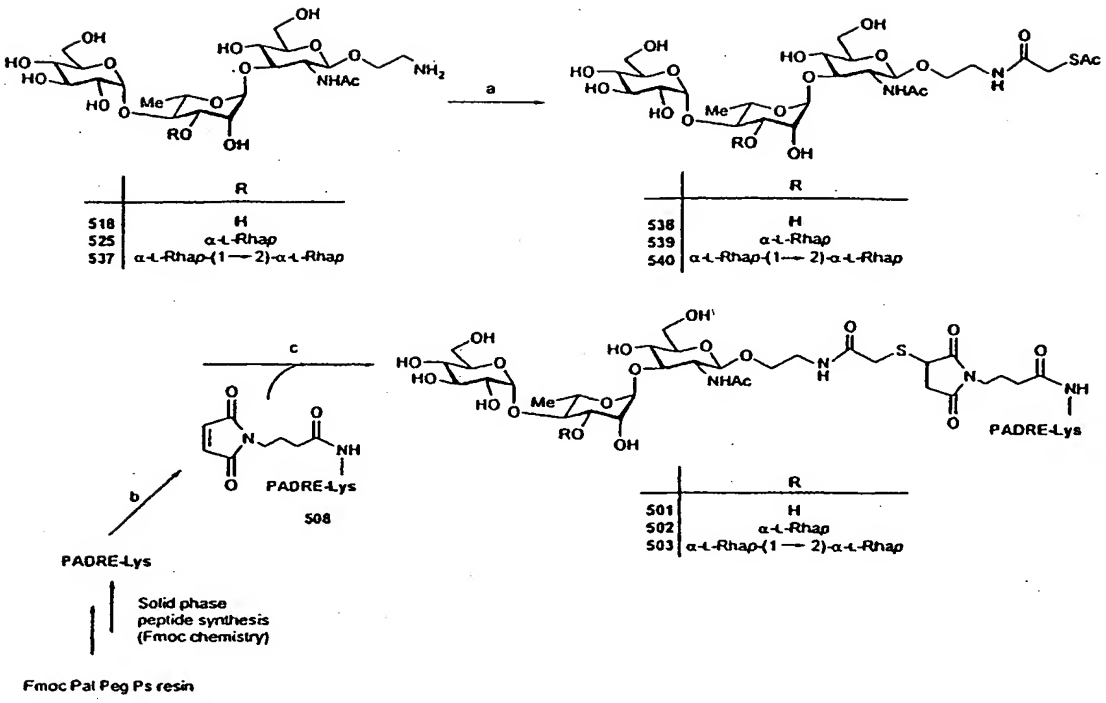

a
b
c
R
518 H
525 α-L-Rhap
537 α-L-Rhap-(1→2)-α-L-Rhap
538 H
539 α-L-Rhap
540 α-L-Rhap-(1→2)-α-L-Rhap
501 H
502 α-L-Rhap
503 α-L-Rhap-(1→2)-α-L-Rhap
PADRE-Lys
508
PADRE-Lys
Solid phase peptide synthesis (Fmoc chemistry)
Fmoc Pal Peg Ps resin

FIGURE 23

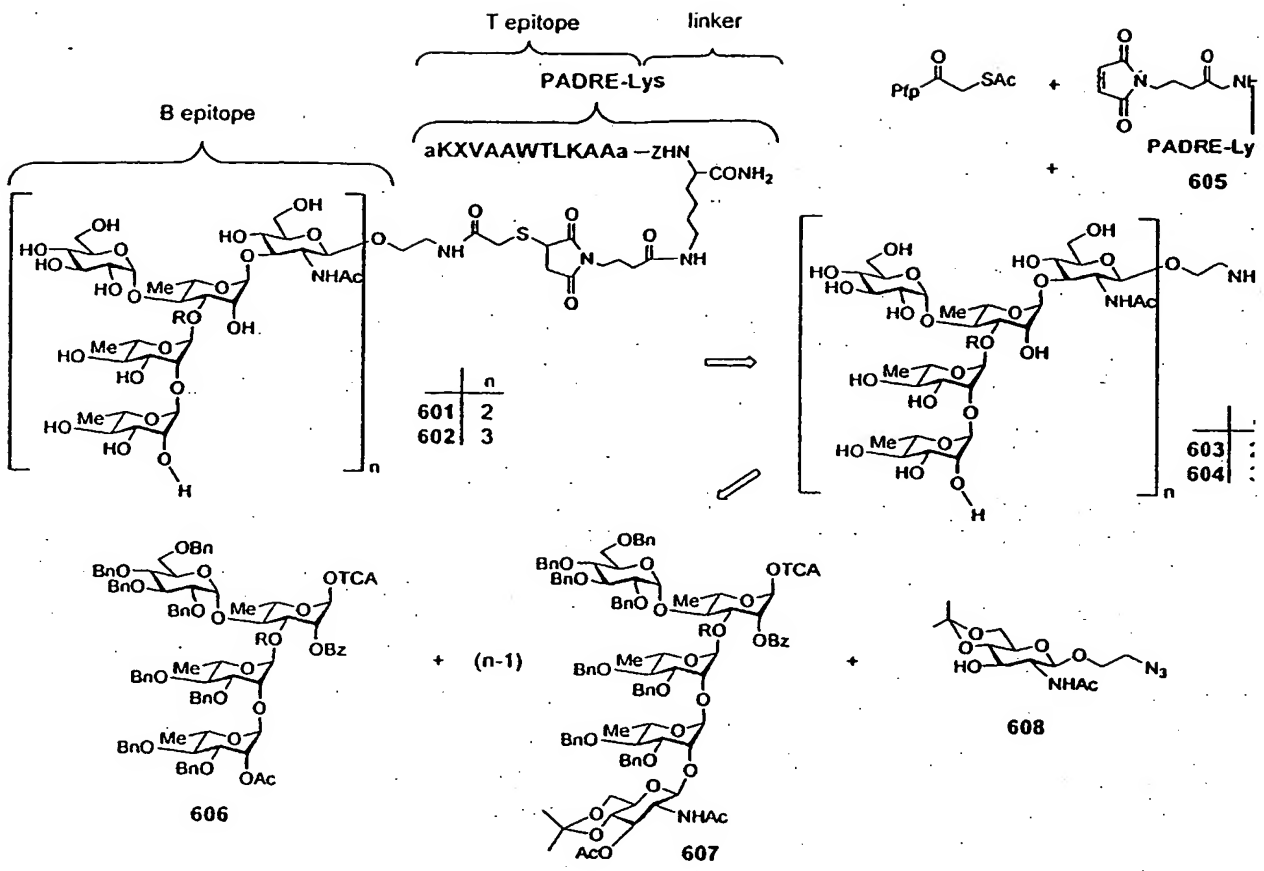


FIGURE 24

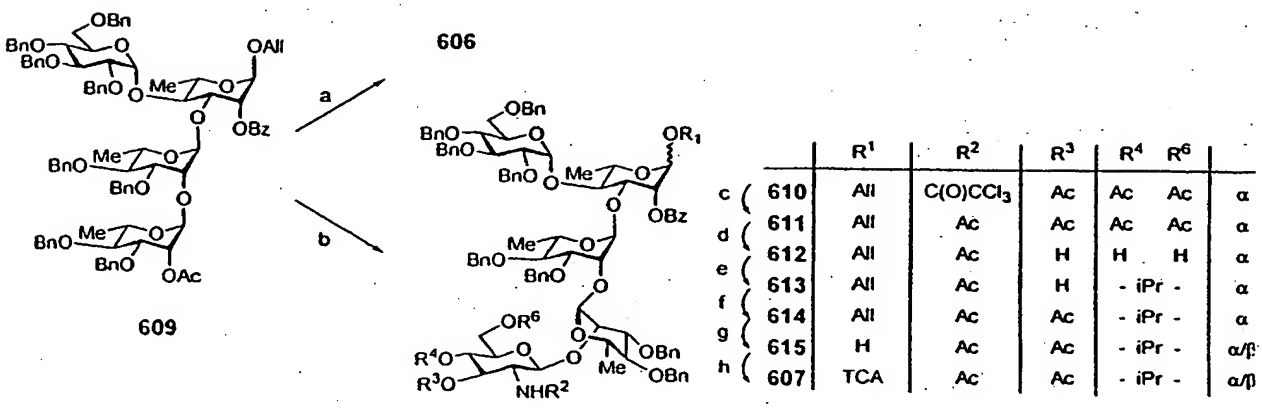
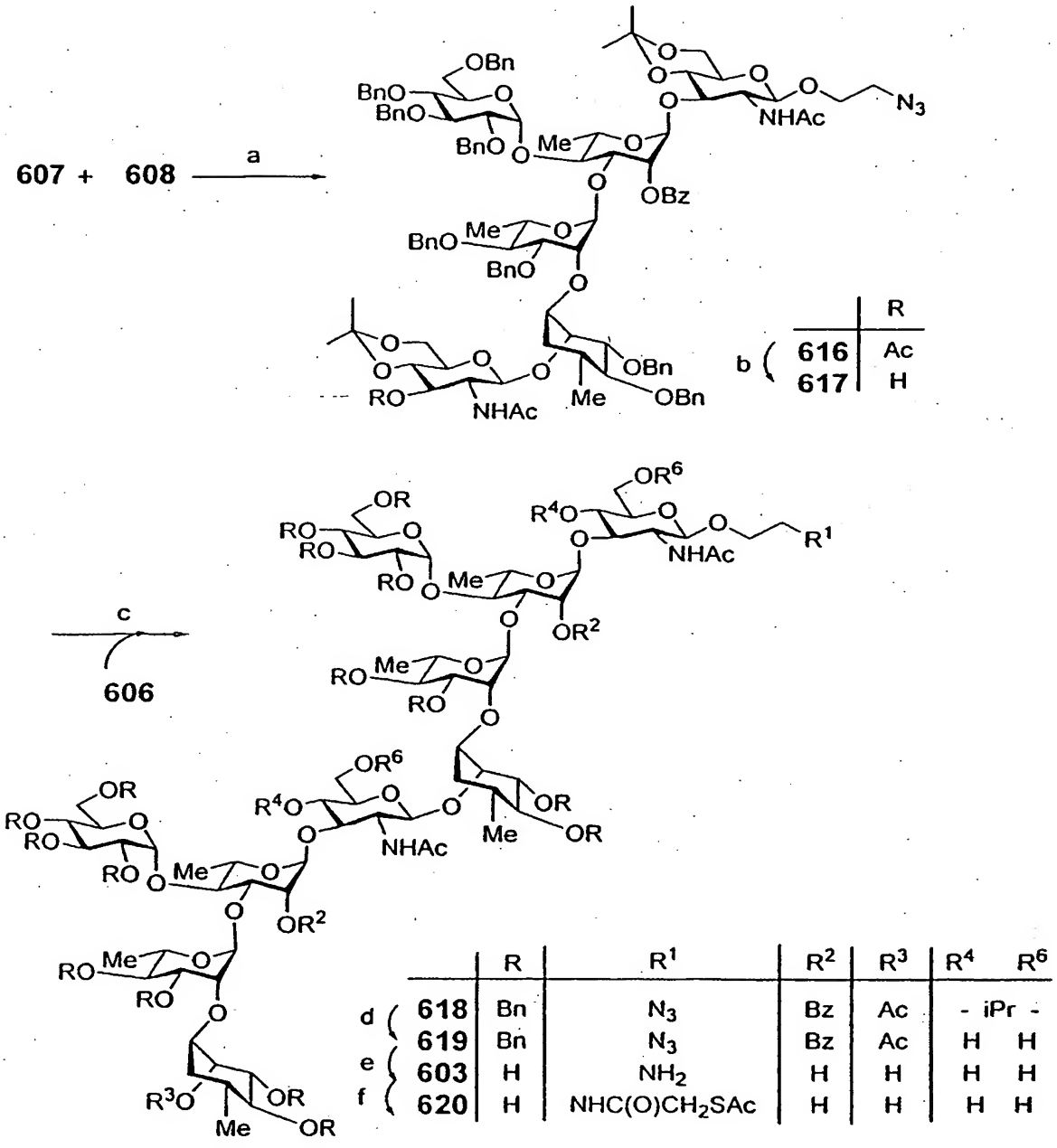


FIGURE 25



		R	R1	R2	R3	R4	R6
b	616	Ac					
b	617	H					
d	618	Bn	N_3	Bz	Ac	- iPr -	
d	619	Bn	N_3	Bz	Ac	H	H
e	603	H	NH_2	H	H	H	H
f	620	H	$NHC(O)CH_2SAc$	H	H	H	H

FIGURE 26

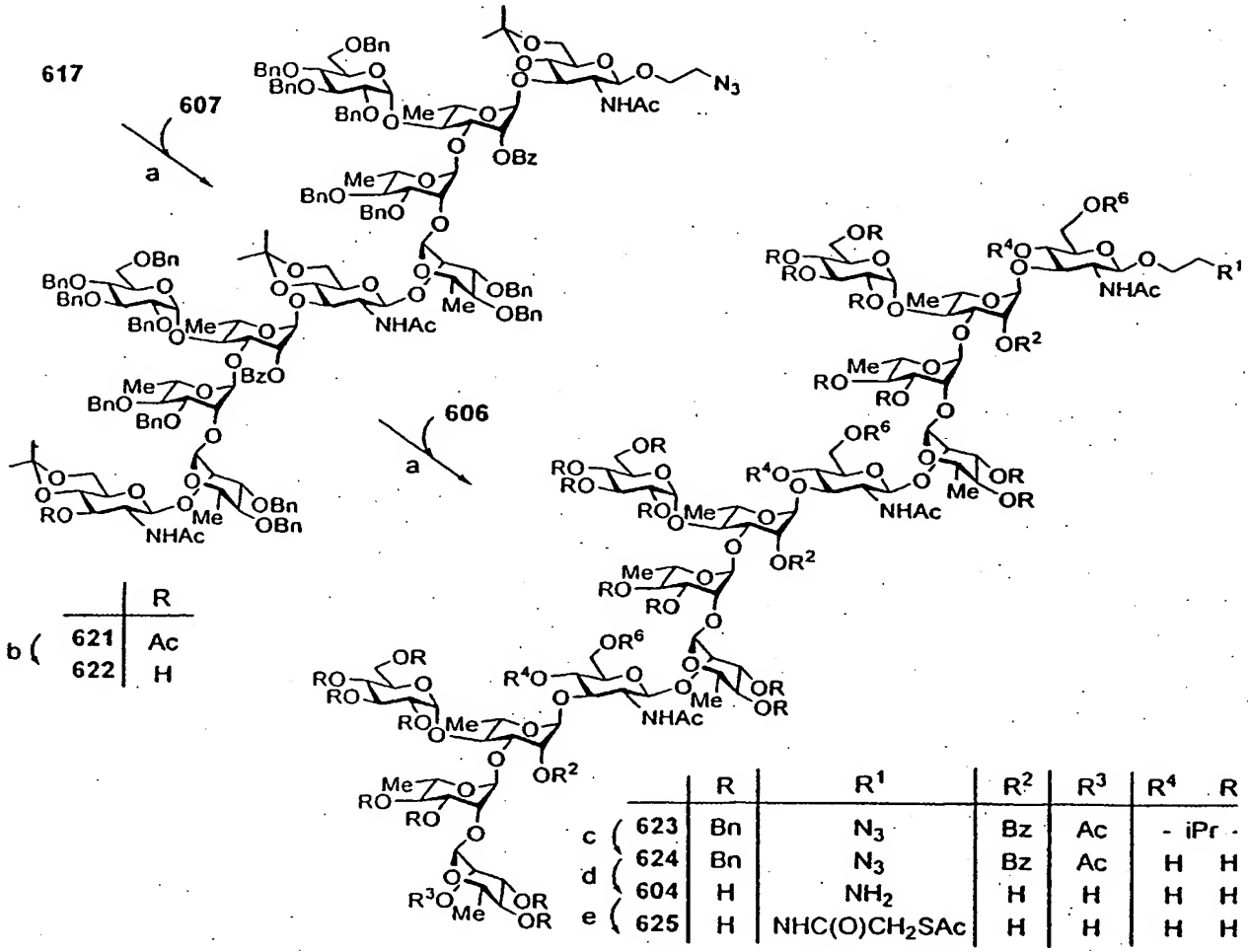
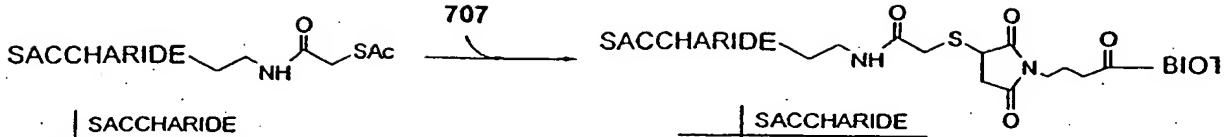
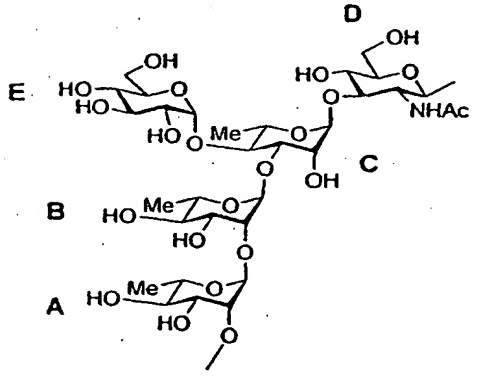

617
607
a
606
a
b
c
d
e
R
621 Ac
622 H
R R1 R2 R3 R4 R
623 Bn N3 Bz Ac - iPr -
624 Bn N3 Bz Ac H H
604 H NH2 H H H H
625 H NHC(O)CH2SAc H H H H

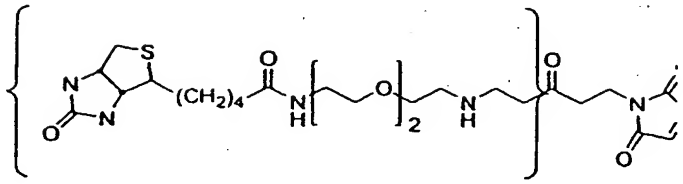
FIGURE 27



	SACCHARIDE
701	ECD
702	B(E)CD
703	AB(E)CD
704	DAB(E)CD
705	$\{AB(E)CD\}_2$
706	$\{AB(E)CD\}_3$

	SACCHARIDE
708	ECD
709	B(E)CD
710	AB(E)CD
711	DAB(E)CD
712	$\{AB(E)CD\}_2$
713	$\{AB(E)CD\}_3$





707

{} = BIOT

FIGURE 28

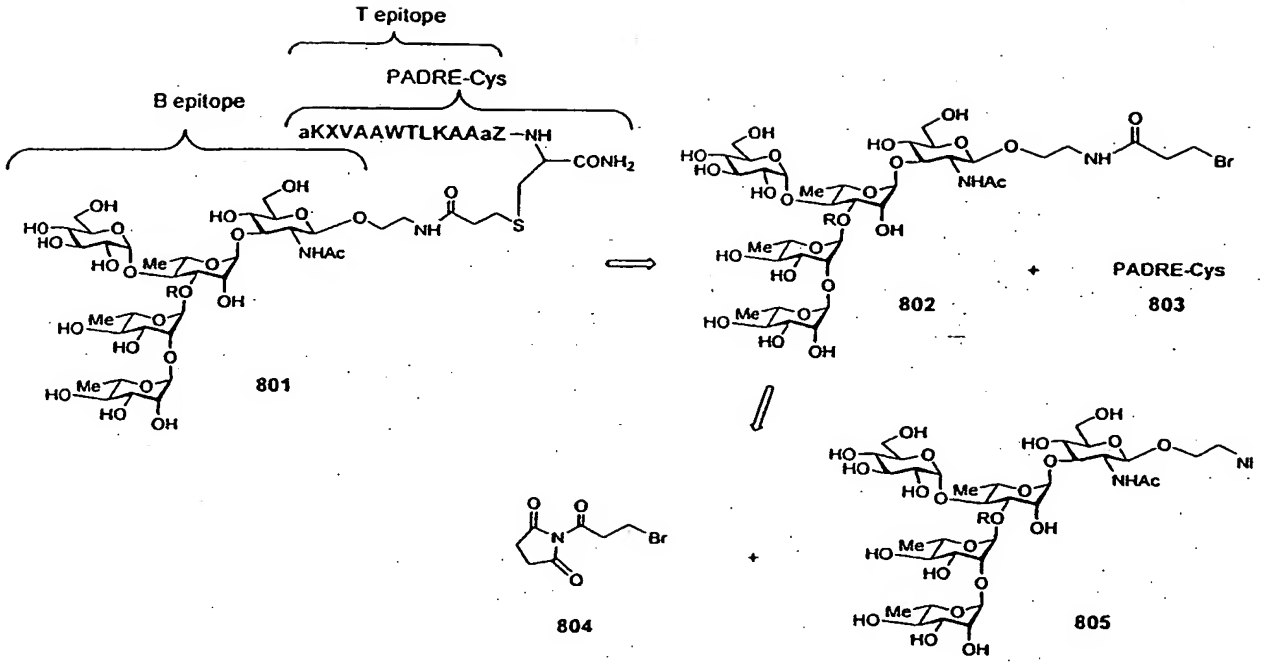
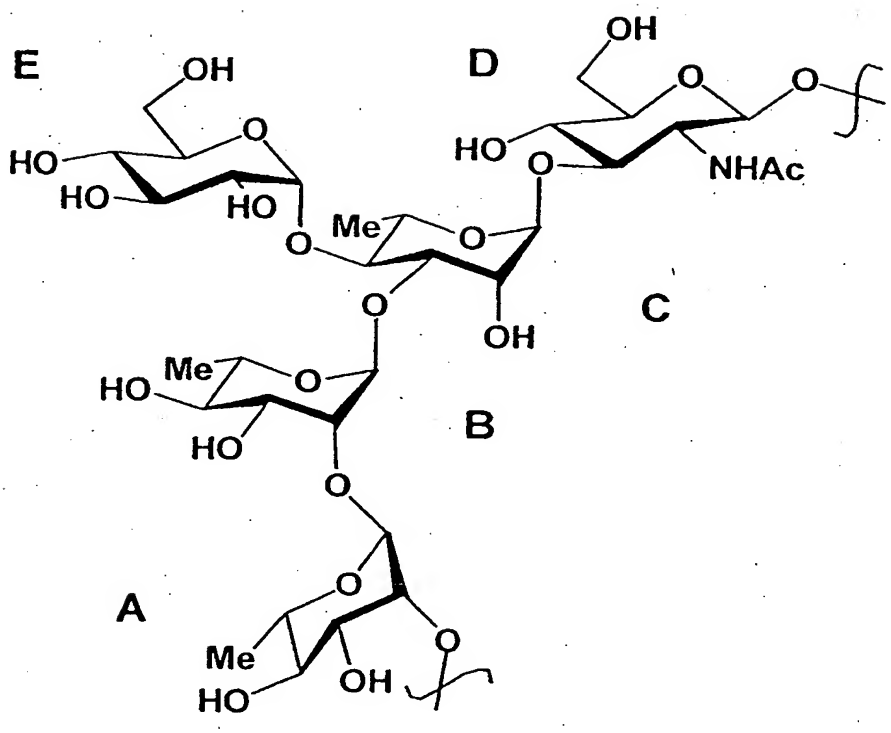


FIGURE 28bis



2)-αLRha*p*-(1,2)-αLRha*p*-(1,3)-[αDGlc*p*-(1,4)]-αLRha*p*-(1,3)-βDGlcNAc*p*-(1
A B E C D

Figure 29

A
Anti-S. flexneri 2a LPS
antibody titer
4000
3000
2000
1000
IgG1
IgG2a
IgG2b
IgG3
B
10exp5 cfu/lungs
1200
800
400
0
control
preimmune
a
b
c
immune

Figure 30

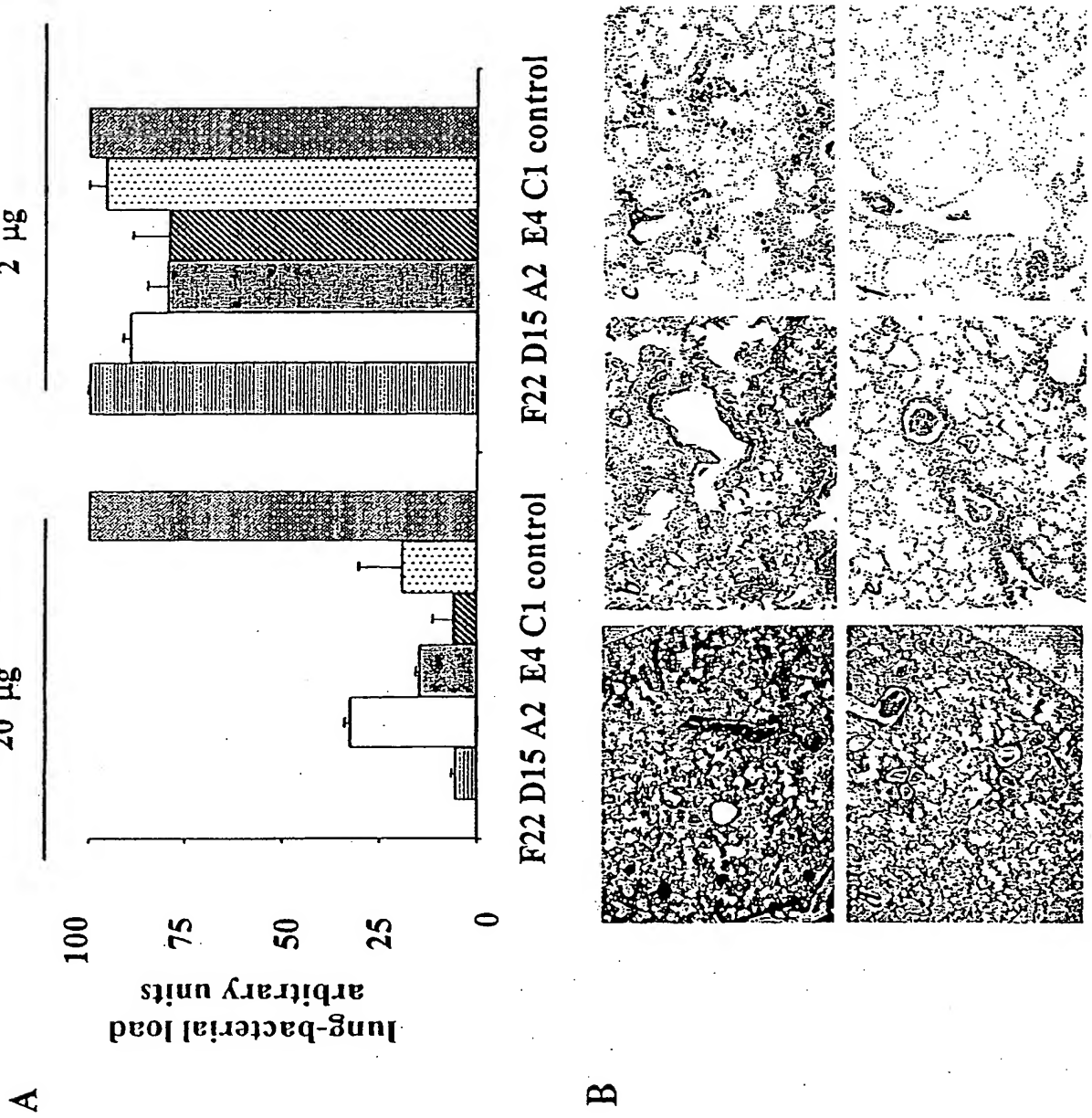
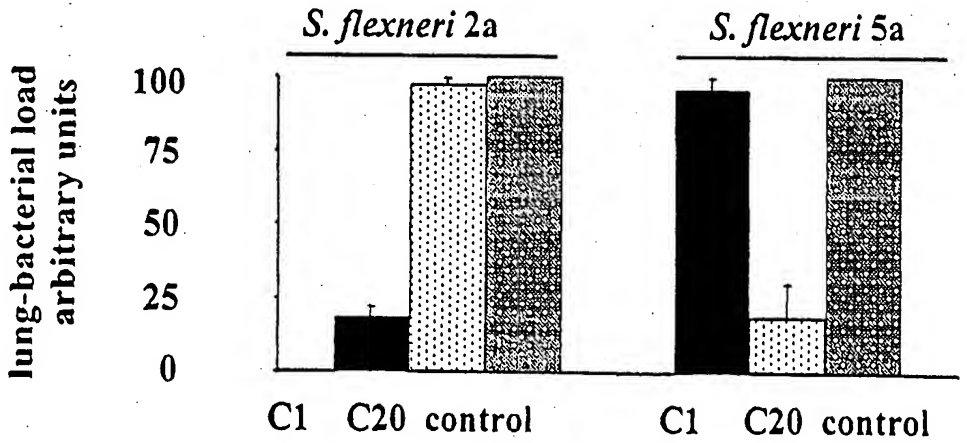

A
B
20 µg
2 µg
lung-bacterial load
arbitrary units
100
75
50
25
0
F22 D15 A2 E4 C1 control
F22 D15 A2 E4 C1 control
a
b
c

Figure 31

A


S. flexneri 2a
S. flexneri 5a
lung-bacterial load
arbitrary units
100
75
50
25
0
C1
C20
control
C1
C20
control

B

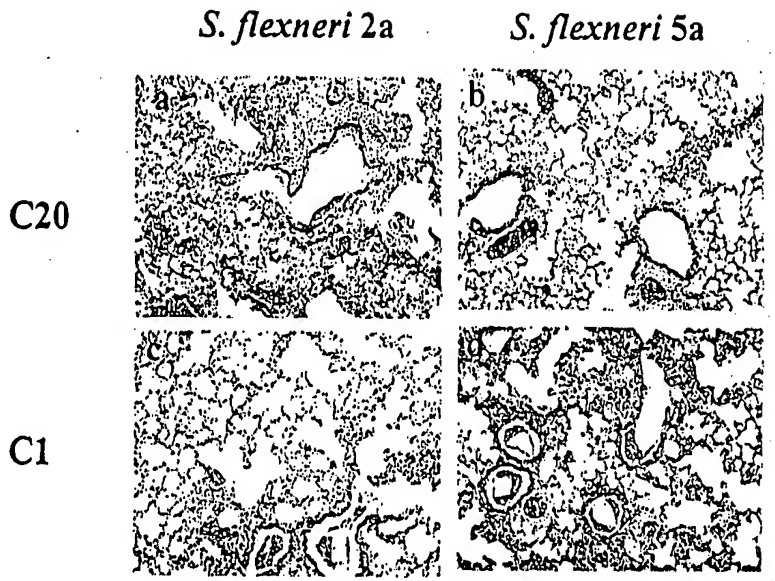

S. flexneri 2a
S. flexneri 5a
C20
C1
a
b
c
d

Figure 32

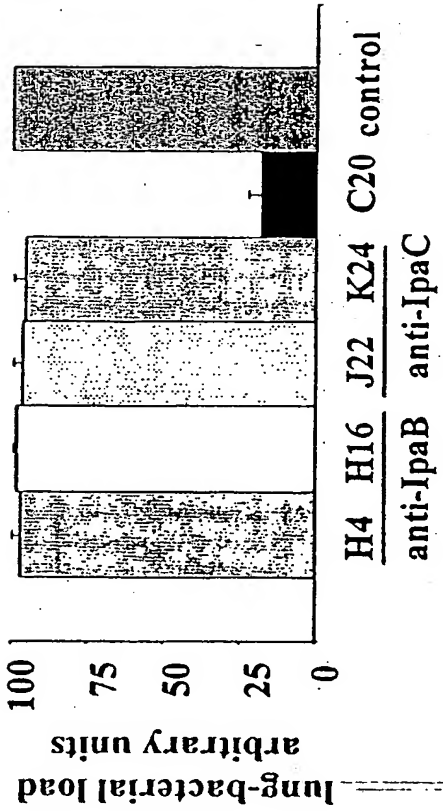

lung-bacterial load
arbitrary units
100
75
50
25
0
H4
H16
J22
K24
C20
anti-IpaB
anti-IpaC
control

Figure 33

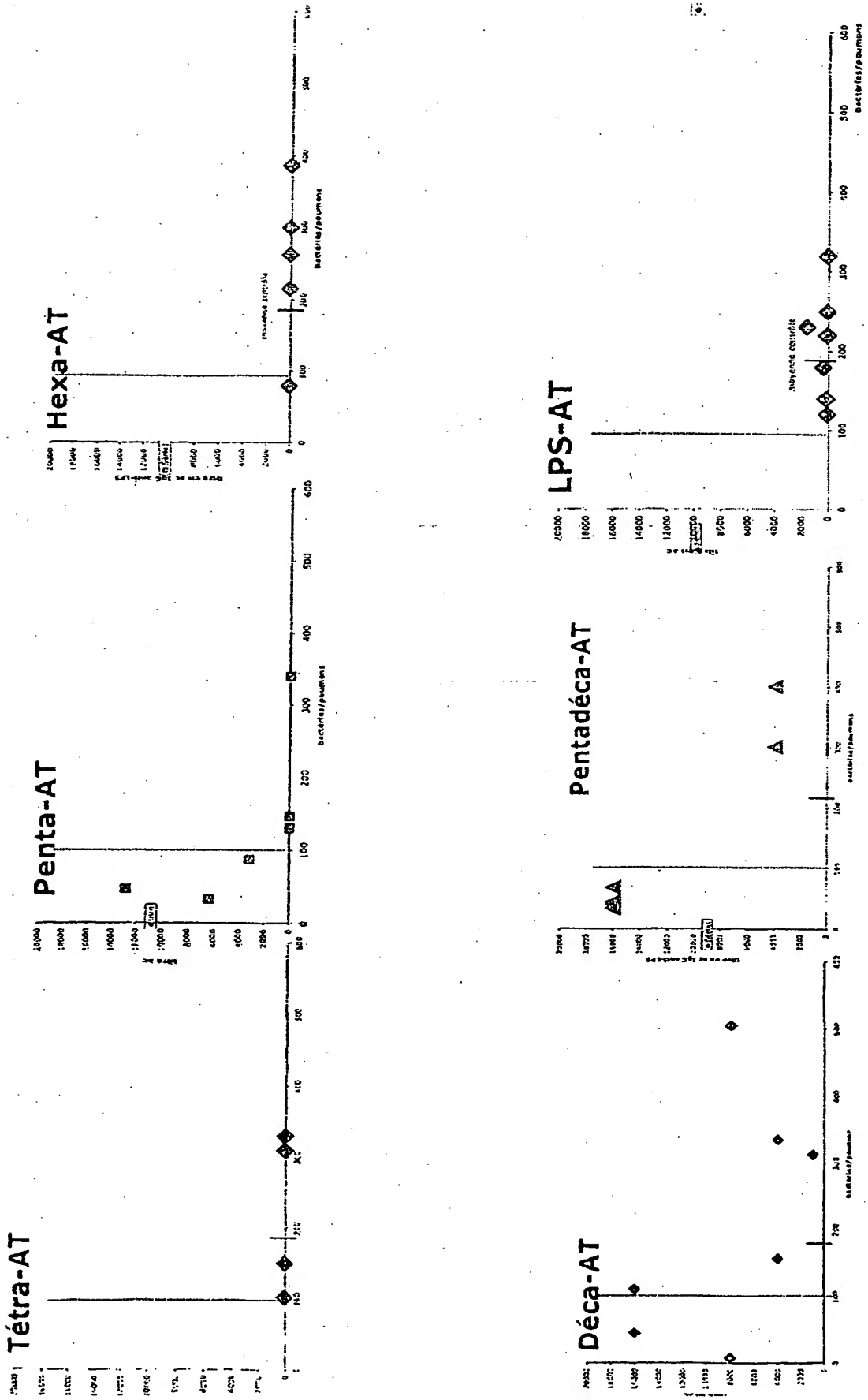


Figure 34